

10/602,413

- 4 -

PCA391-D1-01-CFP

**REMARKS**

Claims 2, 3, 58, and 59 are pending in the application.

Claim 2 is currently amended.

Claims 3, 58, and 59 were previously presented.

***Claim Rejections – 35 USC § 103***

In the Office Action, claims 2 and 3 are rejected under 35 USC § 103(a) as allegedly being unpatentable over Lu et al., J. Pharm. & Exper. Ther., 1999, vol. 290(1): pages 214-219, in view of Minor, Arthritis & Rheumatism, 1996, vol. 9(2): pages 79-81, and the entry for Osteoarthritis in the Merck Manual of Diagnosis and Therapy, 7<sup>th</sup> edition, pages 449-451 (1999). It was stated in the Office Action that Lu et al. teach the use of gabapentin for the relief of nociceptive pain, including arthritic pain, wherein the relief did not relate to improving inflammation. But it was acknowledged in the Office Action that Lu et al. do not teach the use of gabapentin for treating noninflammatory cartilage damage. It was stated in the Office Action that Minor suggests exercise for osteoarthritis (OA) patients and that the Merck Manual mentions that "Exercise (. . .) maintains healthy cartilage," and also that "[i]mmobilization can accelerate and worsen the clinical course [of OA]. Arrest and occasionally reversal of hip and knee OA can occur using well-planned exercise as therapy" (page 451). It was argued in the Office Action that it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the teaching of Lu et al. by administering gabapentin to OA patients who suffered from severe chronic pain that precluded them from engaging in a healthy level of physical activity. It was further stated in the Office Action that the transitional term "comprising" in the claims is open-ended, and as such does not exclude courses of therapy that include administration of gabapentin to a mammal and well-planned exercise of the mammal.

Applicants traverse the rejection of claims 2 and 3 for the reasons provided below. Applicants' remarks below first address why use of the transitional phrase "the method consisting essentially of" is proper, and then why the invention method claimed using the phrase is nonobvious over Lu et al. in view of Minor and the Merck Manual.

**Use of "the method consisting essentially of" is proper**

The transitional term "comprising" in claim 2 has been replaced by the transitional phrase "the method consisting essentially of." The phrase is incorporated into

10/602,413

- 5 -

PCA391-D1-01-CFP

dependent claim 3 from claim 2. This phrase limits the scope of claims 2 and 3 to the respective steps specified therein and to those steps that do not materially affect the basic and novel characteristics of the claimed invention.<sup>1</sup>

Support for the amendment is found in the specification, wherein rehabilitation and analgesic drugs are included in a list of therapies that failed to treat the primary condition of osteoarthritis, which is damage to cartilage.<sup>2</sup> Further support is found in the specification<sup>3</sup> and the original and present claims, wherein it is stated that GABA analogs useful in the present invention method are those having the characteristic of being inhibitors of cartilage damage. Applicants thus contemplated that GABA analogs having the characteristic of being inhibitors of cartilage damage are useful to treat cartilage damage in a patient without additional therapy such as well-planned exercise.

Introducing the well-planned exercise that formed the basis for the rejection would materially change the characteristics of Applicants' invention by, for example, requiring a patient to exercise to treat the patient's cartilage damage. Applicants' invention does not require the patient to exercise to treat the patient's cartilage damage. Thus, for example, some patients are incapable of exercising due to joint stiffness or joint pain that cannot adequately be alleviated by analgesics and yet are able to be treated according to the present invention method, whereas such patients would not be treatable according to a method that required them to exercise as part of their treatment.

In the Office Action, it was further argued that nowhere in Applicants' disclosure is it stated that the claimed cartilage-preserving effect is a result of treatment by a GABA analog having the characteristic of being an inhibitor of cartilage damage and not the result of exercise. In fact the opposite is true: Applicants state in the specification that the results for gabapentin in the EOA rabbit model that are presented in Tables 1-4 indicate that gabapentin reduced cartilage damage.<sup>4</sup>

In the Office Action, it was acknowledged that the EOA rabbit model of Biological Method 1 demonstrated that animals administered gabapentin displayed a reduced amount of cartilage damage, but it was alleged that the model failed to control for the

<sup>1</sup> Manual of Patent Examining Procedure, 8<sup>th</sup> ed. Incorporating revision no. 2, 2004, §2111.03, page 2100-52, second column.

<sup>2</sup> Specification, page 1, line 23, to page 2, line 4

<sup>3</sup> Specification, page 3, lines 3 to 7

<sup>4</sup> Specification, page 208, lines 17-28

10/602,413

- 6 -

PCA391-D1-01-CFP

amount of physical activity performed by treated versus untreated rabbits and it was speculated that this control is relevant to the model.

Applicants respectfully disagree. As mentioned above, the claims relate to methods of treating using GABA analogs having the characteristic of being inhibitors of cartilage damage, and Applicants point out in the specification that exercise such as athletic activities typically lead to cartilage damage.<sup>5</sup> Applicants believe this is why the Merck Manual calls for well-planned exercise.

Further, there is no evidence presented in the Office Action for the speculation that the non-specific exercise mentioned for the EOA rabbit model resulted in a beneficial effect on cartilage. There is no basis to expect that the rabbits used in the experiments engaged in well-planned exercise. Rather, since exercise may lead to cartilage damage, the exercise referenced in the specification is more likely to have had no effect on, or even worsened, the rabbits' cartilage damage, thus supporting more a counter argument to that given in the Office Action.

Further, there is no evidence in the Office Action for the speculation that gabapentin treated animals engaged in different levels of exercise than untreated ("OA (water)") animals, or that the beneficial effects observed with gabapentin were due to exercise and not due to gabapentin's pharmacological effects. Rather, the opposite is true: Applicants state in the specification that the results for gabapentin in the EOA rabbit model that are presented in Tables 1-4 indicate that gabapentin reduced cartilage damage.<sup>6</sup>

Accordingly, Applicants believed that the EOA rabbit model was predictive of the pharmacological effects of gabapentin on cartilage damage without controlling for exercise of treated and untreated rabbits.

For the reasons given above, Applicants believe that use of the transitional phrase "the method consisting essentially of" in claims 2 and 3 is proper, and thus that the exercise of Minor and the Merck Manual is excluded from the scope of claims 2 and 3.

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<sup>5</sup> Specification, page 1, lines 5 to 9

<sup>6</sup> Specification, page 208, at lines 17-28

10/602,413

- 7 -

PCA391-D1-01-CFP

Claims 2 and 3 with "the method consisting essentially of" are nonobvious

Applicants believe that claims 2 and 3 are nonobvious because:

1. there was no reasonable expectation of success for using gabapentin without well-planned exercise to treat noninflammatory cartilage damage at the time the present application was filed; and, independently,
2. the present invention omits a required element of Lu et al. in view of Minor and the Merck Manual, and omission of an element with retention of the element's function is an indication of unobviousness.

#### 1. NO REASONABLE EXPECTATION OF SUCCESS

Minor and the Merck Manual mention exercise therapy for OA and Lu et al. mention gabapentin for treating nociceptive arthritic pain. But Applicants believe that Lu et al. in view of Minor and the Merck Manual do not teach or suggest any pain relieving medication for treating noninflammatory cartilage damage without well-planned exercise.

Noninflammatory cartilage damage is a "disorder of hyaline cartilage and subchondral bone characterized by hypertrophy of tissues in and around the involved joints, which may or may not be accompanied by deterioration of hyaline cartilage surface."<sup>7</sup> Noninflammatory cartilage damage is a pathological effect distinct from arthritic pain, which is a symptom.

Lu et al. provide no evidence (e.g., experimental data or literature references) suggesting that gabapentin for treating any type of cartilage damage without well-planned exercise would be successful. Minor and the Merck Manual do not cure the deficiency of Lu et al. because they also fail to provide any such evidence.

Applicants believe that such evidence is required for a proper obviousness rejection.<sup>8</sup> In a case on point, the Federal Circuit in *In re O'Farrell* characterized prior art references, known as the Polisky reference and the Bahl reference, as follows:

"We agree with the board that appellants' claimed invention would have been obvious in light of the Polisky reference alone or in combination with Bahl within the meaning of §103. Polisky contained detailed enabling methodology for practicing the claimed invention, a

<sup>7</sup> Specification, page 44, lines 1-4

<sup>8</sup> In re O'Farrell, 853 F.2d 894, 903, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988); cited in the Manual of Patent Examining Procedure, 8<sup>th</sup> ed. Incorporating revision no. 2, 2004. §2145 (X)(B), page 2100-161.

10/602,413

- 8 -

PCA391-D1-01-CFP

suggestion to modify the prior art to practice the claimed invention, and evidence suggesting that it would be successful. "(7 USPQ2d 1680 , first column, last paragraph; emphasis added).

"The information in the Polisky reference, when combined with the Bahl reference provided such a reasonable expectation of success." (7 USPQ2d 1681, first column, last complete paragraph)

But Lu et al. in view of Minor and the Merck Manual do not provide evidence suggesting that the use of gabapentin for treating noninflammatory cartilage damage without well-planned exercise would be successful. Thus, Applicants believe that claims 2 and 3 are nonobvious because there was no reasonable expectation of success for using gabapentin to treat noninflammatory cartilage damage without well-planned exercise at the time the present application was filed.

## 2. OMISSION OF AN ELEMENT WITH RETENTION OF THE ELEMENT'S FUNCTION IS AN INDICATION OF UNOBVIOUSNESS

As noted above, it was argued in the Office Action that Lu et al. in view of Minor and the Merck Manual suggest a combination therapy of using gabapentin for arthritic pain relief and well-planned exercise therapy for treating cartilage damage of OA.

In contrast the present invention omits the element of well-planned exercise and retains the element's function of treating cartilage damage. Omission of an element with retention of the element's function is an indication of unobviousness.<sup>9</sup> Thus, Applicants also believe that claims 2 and 3 are nonobvious because the invention of claims 2 and 3 omits the exercise element of Lu et al. in view of Minor and the Merck Manual and retains the element's function of treating cartilage damage, which is noninflammatory cartilage damage in the invention of claims 2 and 3.

Accordingly in view of the above remarks, Applicants believe that claims 2 and 3 are not obvious over Lu et al. in view of Minor and the Merck Manual, and are patentable under 35 U.S.C. § 103(a).

### ***Claim Rejections - 35 USC § 101 Double Patenting***

Claims 58 and 59 are rejected under 35 USC § 101 as allegedly claiming the same invention as that of claims 4 or 5, respectively, of U.S. Patent No. 6,620,829.

<sup>9</sup> Manual of Patent Examining Procedure, 8<sup>th</sup> ed. Incorporating revision no. 2, 2004. §2144.04 (II)(B), page 2100-139

10/602,413

- 9 -

PCA391-D1-01-CFP

Applicants traverse the rejection because claims 4 and 5 of US 6,620,829 are not the same invention as what is being claimed in instant claims 58 and 59. Claims 4 and 5 of US 6,620,829 relate to methods of treating using compounds, whereas instant claims 58 and 59 relate to methods of treating using pharmaceutical compositions comprising the compounds and a pharmaceutically acceptable carrier, diluent, or excipient. Thus the instant claims are not co-extensive in scope with the claims of US 6,620,829. Accordingly, Applicants believe that the rejection of claims 58 and 59 for same invention double patenting is overcome and that claims 58 and 59 are patentable under 35 USC § 101 over US 6,620,829.

#### **Conclusion**

In view of the above amendments and remarks, Applicants believe that the rejections are overcome and that claims 2, 3, 58, and 59 are patentable. Applicants request reconsideration and allowance of claims 2, 3, 58, and 59.

The present reply is being mailed or transmitted within two months of the mailing date of the Office Action. Should any rejections be maintained after reconsideration of the claims, Applicants hereby request that an Advisory Action be timely issued.

The undersigned can be reached by telephone or facsimile at the numbers provided below.

Respectfully submitted,

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